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Attention deficit hyperactivity disorder in the diabetic population: relationship with metabolic syndrome and atherogenic index of plasma

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ABSTRACT

Aims: The objective of the current study is to investigate the prevalence of Attention Deficit/Hyperactivity Disorder (ADHD) among individuals diagnosed with diabetes mellitus (DM). Additionally, this study aims to evaluate the potential association between ADHD and metabolic syndrome (MetS), atherogenic index of plasma (AIP), and other lipid parameters, considering the different types of DM.

Methods: The study comprised 213 adult patients diagnosed with diabetes mellitus, consisting of 120 females and 93 males. Participants completed the Adult Attention Deficit Hyperactivity Disorder Self-Report Scale (ASRS) as a screening tool for symptoms. The study assessed many physiological indicators, including body mass index, waist circumference, blood pressure, glucose levels, cholesterol levels, high-density lipoprotein levels, low-density lipoprotein levels, triglyceride levels, uric acid levels, and glycated hemoglobin levels.

Results: The study yielded a prevalence rate of 10.7% for ADHD among diabetes individuals. The prevalence of ADHD was found to be more common in individuals diagnosed with type 1 diabetes mellitus (T1DM) compared to those with type 2 diabetes mellitus (T2DM), with rates of 15.4% and 9.8% respectively. The study revealed that individuals diagnosed with T2DM who also had MetS, organ involvement, concurrent disorders, and stress-related eating had significantly higher scores on the ASRS/T scale. There was a correlation observed between the ASRS-HI and AIP levels in individuals diagnosed with T2DM. The statistical analysis revealed that ADHD-HI and T scores significantly influenced the severity of MetS. A progressive increase in ASRS/T and ASRS/I scores was observed with the duration of DM.

Conclusion: In conclusion, by recognizing and treating accompanying neuropsychiatric conditions such as ADHD symptoms in diabetic patients, individuals may exhibit improved adherence to lifestyle modifications and antidiabetic therapies. This approach potentially reduces the risks of acute and chronic complications, including cardiovascular risk, through the enhanced management of DM.

Keywords: Diabetes mellitus, attention deficit hyperactivity disorder, metabolic syndrome, atherogenic index of plasma

INTRODUCTION

Diabetes mellitus (DM), one of the most significant public health diseases of the 21st century, impacting millions of individuals worldwide, is the most common endocrine disorder. The estimated prevalence of the condition is approximately 463 million, with projections indicating a potential increase to 700 million by 2045.[1] This chronic illness substantially impacts individuals' quality of life, necessitating a considerable allocation of medical and economic resources.

In recent studies, it has been demonstrated that DM affects glucose metabolism and other physiological systems. The effects of diabetes on metabolic health, both acute and chronic organ complications, are well known. For instance, metabolic syndrome (MetS) accompanying DM may indicate a more complex and severe clinical course for patients. In addition, it is reported that diabetes may also affect neurological and psychiatric functions. In this context, investigation of neurological and psychiatric comorbidities associated with DM is becoming increasingly important.

In recent studies, evidence has emerged indicating a potential correlation between DM and behavioral disorders, specifically attention deficit hyperactivity

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disorder (ADHD).[2] ADHD is a neurodevelopmental disorder characterized by inattention, hyperactivity, and impulsivity incompatible with the development level, often leading to impairments in social, academic, and occupational functionality. The etiology of ADHD is not fully understood, but an essential etiological factor is that, as in diabetes, the genetic component predominates.[3] The likelihood of ADHD is increased by two to fourfold in first-degree relatives of children with ADHD.[4] Similarly, the likelihood of diabetes is increased by four to sixfold higher in first-degree relatives of individuals with Type 2 DM (T2DM).[5] ADHD affects 2.6% of the global population,[6] reported to be 4.2% in rich-resource countries and 1.9% in poor-resource countries, increasing over the years.[7] ADHD symptoms typically appear in early childhood, and about half of the disease persists into adulthood. With the adoption of the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) criteria in 2013, ADHD is now recognized not as a childhood disease but as a chronic disease that persists throughout life.[8] Hypoactivity of dopamine (DA) and norepinephrine in frontal-subcortical circuits in ADHD forms the basis of brain and functional dysfunction in ADHD.[9] DA and norepinephrine exhibit neuromodulatory effects on behavior and cognition via the fronto-striato-cerebellar circuit pathway.[10] Further research is needed to elucidate the molecular mechanisms linking DM-associated dopaminergic dysfunction and cognitive impairment and evaluate glucotoxicity's detrimental effects. Animal studies have reported that hyperglycemia and relative insulin deficiency promote neurodegeneration by impairing dopaminergic neurotransmission.[11] Recent reports suggest that advanced glycation end products and their precursor methylglyoxal are associated with cognitive impairment and changes in the dopaminergic system.[12,13] Considering the crucial role of insulin and glucose in DA homeostasis, it is not surprising that dopaminergic function is altered in DM.[14]

It is also known that individuals with T2DM have significant impairments in visual and verbal memory, attention and concentration, processing speed, executive function, and motor control.[15] ADHD has been found to be correlated with systemic inflammation, a significant factor in the pathogenesis of atherosclerosis, as observed in numerous diseases. The atherogenic index of plasma (AIP) is a parameter used as an indicator of cardiovascular risk calculated based on plasma triglyceride (TG) and high density lipoprotein (HDL) levels, assessing the possibility of atherogenic status with lipid profile. A recent large-scale study reported that plasma TG levels increased while HDL levels decreased in individuals with ADHD.[16] These findings have led to the need to evaluate the potential cardiovascular risk of ADHD using the AIP. The prevalence of ADHD has been documented to be higher in patients diagnosed with T1DM and T2DM. However, the precise mechanisms of this relationship remain yet unknown. In a large-scale study, it was reported that adolescents and young adults with ADHD were approximately three times more susceptible to developing T2DM.[17] It is thought that ADHD might increase the risk of DM, and DM could exacerbate ADHD symptoms. Impulsive behaviors, self-regulation, and self-motivation problems may be risk factors for the development of abnormal eating, such as overeating, which can lead to DM and obesity. It has been demonstrated that individuals diagnosed with T1DM exhibit a heightened vulnerability to psychiatric disorders, such as ADHD.[18,19] The fact that T1DM is a neurodevelopmental disorder like ADHD, immune system damage, and inflammatory processes predispose to the development of ADHD. The management of T1DM requires more adequate cognitive and manual dexterity compared to T2DM in carbohydrate counting and calculation of insulin correction doses. Research has demonstrated that patients co-diagnosed with ADHD and T1DM have poorer metabolic control, and diabetic ketoacidosis is twice as common as those without ADHD.[20] Several studies have found a reduction in white matter volume, particularly in the frontal region, in individuals diagnosed with T2DM. This region is responsible for various cognitive tasks, including attention, cognition, and motor activity.[21,22] Therefore, this phenomenon may potentially increase the susceptibility of ADHD by eliciting symptoms of inattentiveness and impulsivity. The similarity of hereditary transmission rates and potential factors in pathogenesis- including dysfunction of the dopaminergic system, insulin resistance, obesity, abnormal eating patterns, predisposition to MetS, and neurodevelopmental characteristics are the common characteristics of DM and ADHD currently being investigated.

The objective of our research is to investigate and compare the prevalence and severity of ADHD in T1DM and T2DM and to evaluate the potential association between ADHD and MetS, AIP, and other lipid parameters, considering the being T1DM or T2DM. Ultimately, recognizing ADHD symptoms that negatively affect diabetes regulation and providing appropriate intervention may be crucial for diabetes treatment. In addition, early initiation of lifestyle changes that might reduce the risk of T2DM and MetS in patients with ADHD will form the basis of preventive and therapeutic holistic approaches.

METHODS

Two hundred and thirteen patients with diabetes mellitus (120 females and 93 males) admitted to the outpatient clinic of Endocrinology and Metabolism Diseases, Erzurum Health Science University Training and Research Hospital between June 2023 and October 2023 were involved in this prospective crossectional study. Our study focused on the clinical characteristics and biochemical parameters of 213 adult participants with DM. The study protocol received approval from the Ethics Committee of Erzurum Training and Research Hospital, with a decision number 02/16, dated 14.06.2023. All participants provided written and verbal informed consent. The research was conducted in accordance with the ethical guidelines outlined in the Declaration of Helsinki. The patients filled out the sociodemographic, clinical data form and the Adult Attention Deficit Hyperactivity Disorder Self-Report Scale (ASRS) to screen ADHD symptoms. Participants' weight, height, waist circumference, and blood pressure were measured. The diagnostic criteria for Metabolic Syndrome (MetS) employed the guidelines established by the National Cholesterol Education Program Adults Treatment Panel-III.[23] The following formulas were used. The severity of MetS was calculated based on the number of positive criteria.

BMI= Weight (kg)/ Height (m)^2

AIP= log10 (Triglyceride /HDL ratio),

The criteria for inclusion in the present study were established as follows: individuals must have a confirmed diagnosis of diabetes mellitus, be within the ages of 18 to 65 years, have fundamental literacy skills, and not have any physical or mental disabilities that might impede their ability to complete the required assessments. Additionally, they should give their written consent to be involved in the study. Pregnant women, patients with renal failure, cancer, another cognitive disorder, major psychiatric diagnosis, receiving psychotropics, and alcohol or drug addiction were excluded from the study.

Data Collection Tools

Sociodemographic-clinical data form: It is a form developed by researchers to document the characteristics of participants, including age, gender, body mass index (BMI), and waist circumference. (WC)

Adult Attention Deficit Hyperactivity Disorder Self-Report Scale (ASRS): The screening tool for adult ADHD symptoms has been developed by the World Health Organization. The scale consists of nine items on Inattention (ASRS-I) and nine on hyperactivity/impulsivity (ASRS-H/I). There are 18 questions that evaluate ADHD symptoms. The Likert-type scale employed in this study consists of five points, aiming to assess the frequency of occurrence for each symptom throughout the preceding six-month period. The study on validity and reliability in the Turkish context was conducted by Doğan et al.[24] The scale's internal consistency was determined to be 0.88 during the reliability investigation. The Cronbach's Alpha coefficients for the Inattention and Hyperactivity/Impulsivity subscale are 0.82 and 0.78, respectively. The study observed a test-retest consistency of 0.85 for total scores and 0.73 and 0.89 for subscales, respectively. Those who scored 24 or above from any of the subscales points were considered to have "highly likely ADHD," those who scored 17-23 points were supposed to have "possible ADHD," and those who scored 0-16 points were considered not to have ADHD.[25]

Blood Samples

A series of biochemical tests were conducted. Blood samples were collected from the participants during the fasting period, specifically between the hours of 08:00 and 10:00. Following a period of rest in a seated position, the patients had measurement of routine biochemical parameters in the antecubital region using a vacutainer, administered by experienced health personnel. A sample of blood was collected into a biochemistry tube to measure the levels of glucose, cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL), triglyceride (TG), uric acid, and glycated Hemoglobin (HbA1c). The spectrophotometric approach was used to investigate glucose, cholesterol, HDL, LDL, TG, and uric acid levels. This analysis was conducted using an Atelica clinical chemistry analyzer manufactured by Siemens in Germany. The HbA1c levels were measured by employing the high-performance liquid chromatography technique on the Lifotronic H9 HbA1c device (Lifotronic H9, China)

Statistical Analysis

SPSS 22.0 (SPSS Inc., Chicago, IL, the USA) Statistical software was used for all analyses. Before starting the analyses, a normality test was performed. Frequency analysis was performed to obtain descriptive information about the study's variables. The Student's t-test and the Mann-Whitney U Test were used to compare normally and non-normally distributed variables in comparisons of two independent groups. The ANOVA test was employed for comparing continuous variables across several independent groups, provided that the normal distribution assumption was met. Following the completion of the ANOVA test, subsequent post-hoc analyses were performed. Specifically, the Bonferroni test was employed when the

variances exhibited homogeneity, whereas Tamhane's T2 test was used in cases where the variances did not demonstrate homogeneity. The Pearson Chi-square test was employed for 2x2 comparisons, including categorical variables when the expected value > 5. Conversely, the Chi-square Yates test was used when the predicted value fell within the range of 3-5. Fisher's Exact test was employed if the anticipated value was <3. In comparing categorical variables with dimensions larger than 2x2, the Pearson Chi-square test was used when the expected value was> 5. In contrast, the Fisher-Freeman-Halton test was used when the predicted value was below 5. When comparing two quantitative variables, the Pearson correlation coefficient was employed when the assumption of normal distribution was met. Alternatively, the Spearman correlation coefficient test was utilized if this assumption was not met. In multivariate analysis, previous analyses used linear regression analysis to identify the estimated risk factors between groups. A significance level of $p<0.05$ was utilized for statistical analysis.

RESULTS

A total of 213 patients, 120 females (18 with T1DM, 102 with T2DM) and 93 males (21 with T1DM, 72 with T2DM), were included in the study. Thirty-nine patients were T1DM (18.3%), and 174 (81.7%) were T2DM. The average age of the patients was 50.48±13.73 (29.24±10.05 in T1DM patients, 55.24±9.18 in T2DM patients). According to ASRS, 23 (10.8%) of the participants had highly probable ADHD symptoms, 53 (24.9%) had probable ADHD symptoms, and 137 (64.3%) had no ADHD symptoms. One hundred fifty-five of the patients were diagnosed with metabolic syndrome. Four patients with MetS diagnosis were in the T1DM group, while 151 were in the T2DM group.

Table 1. Comparison of sociodemographic variables in type 1 and type 2 diabetes mellitus

	T1DM n=39 (%)	T2DM n=174 (%)	Total n=213 (%)	p
Gender				
Female	18 (46.2)	102 (58.6)	120 (56.3)	0.215
Male	21(53.8)	72 (41.4)	93 (43.7)	
MetS				
Yes	4 (10.3)	151 (86.8)	155 (72.7)	0.001*
No	35 (89.7)	23 (13.2)	58 (27.3)	
ADHD symptoms				
High likely	6 (15.4)	17 (9.8)	23 (10.7)	
Probable likely	16 (41)	37 (21.3)	53 (24.8)	0.010*
Not likely	17 (43.6)	120 (69)	137 (64.3)	
ADHD appearances				
Inattention	6 (15.4)	22 (40.7)	29 (38.1)	
Hyperactive-impulsive	16 (41)	14 (25.9)	22 (28.9)	0.010*
Combined	17 (43.6)	18 (33.3)	25 (32.8)	

Abbreviations: T1DM: Tip 1 Diabetes Mellitus, T2DM: Tip 2 Diabetes Mellitus, ADHD: Adult Attention Deficit Hyperactivity Disorder, MetS: Metabolic syndrome

Sociodemographic variables, presence of MetS, and ADHD symptoms were compared between T1DM and T2DM groups. There was no difference in terms of gender between diabetic groups. MetS was diagnosed in 72.7% (n=155) of all patients. Of the 155 patients with MetS, 151 (97.4%) were in the T2DM group, and 4 (2.6%) were in T1DM group. The prevalence of ADHD was detected as 15.4% in patients with T1DM and 9.8% in those with T2DM. Of all diabetic patients (n=76) who showed symptoms of ADHD, 38.1% had symptoms of inattentive appearance, 28.9% had symptoms of hyperactive-impulsive appearance, and 33% had symptoms of combined appearance. 36.4% of T1DM patients who showed ADHD symptoms had hyperactive-impulsive appearance, 31.8% had inattentive appearance and 31.8%had combined appearance symptoms. In the T2DM group, inattentive appearance symptoms were 40.7%, combined appearance symptoms were 25.9%, and hyperactive-impulsive appearance symptoms were 25.9%.

Table 2. Comparison of ASRS scale scores, clinical and biochemical parameters in type 1 and type 2 diabetic groups

Parameters	T1DM (n=39)	T2DM (n=174)	p
Age (year)	29.24±10.05	55.24±9.18	<.001
BMI (kg/m2)	23.43±4.72	33.75±7.35	<.001
WC (cm)	78.10±10.72	105.04±14.06	<.001
HbA1c	9.50±2.7	7.94±1.63	<.001
Glucose	251.76±118.24	157.94±71.74	<.001
Trigliseride	108±55.92	197.18±115.01	<.001
Cholesterol	171.56±40.66	185.06±42.34	.083
HDL	44.55±9.64	37.24±9.59	<.001
LDL	123.99±34.46	138.51±35	.020
AIP	0.35±0.23	0.67±0.28	<.001
Uric Acid	3.32±1.04	5.11±1.39	<.001
Severity of MetS	1.67±.74	3.65±.99	<.001
ASRS/I	14.69±7.80	11.96±7.20	.036
ASRS/HI	13.74±5.60	10.45±6.55	.004
ASRS/T	28.44±11.80	22.43±12.30	.006

Data presented as mean±standard deviation, Abbreviations: T1DM: Type 1 Diabetes Mellitus, T2DM: Type 2 Diabetes Mellitus, BMI: Body mass index; WC: Waist Circumference, ASRS: Adult Attention Deficit Hyperactivity Disorder Self-Report Scale, ASRS/I: Inattention score, ASRS/HI: Hyperactivity impulsivity score; ASRS/T: Total score; HbA1c: Glycosylated hemoglobin; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; AIP: Atherogenic index of Plasma; MetS: Metabolic Syndrome.

The comparison of ASRS scale scores clinical and biochemical parameters in T1DM and T2DM patients is demonstrated in Table 2. ASRS total and subscale scores of T1DM patients were significantly higher than those of T2DM patients' (ASRS-IA p=.036; ASRS H/I p=.004; ASRS total p=.006). Age, BMI, WC, TG, LDL, AIP, uric acid, and MetS severity were higher in the T2DM group compared to the T1DM group (p<.001). HbA1c, Glucose, HDL-C, ASRS/HI, ASRS/I, and ASRS/T scores were statistically higher in the T1DM group.

Table 3. Independent samples T-test results of ASRS total scale scores in type 2 DM patients according to demographic variables

Demographic variables	ASRS/T $\bar{x}$±SD	P
Stress related eating		
Yes (n=124)	23.9±12.12	0.011*
No (n=50)	18.72±12.07	
Organ involvement		
Yes (n=23)	29.3±10.7	0.004*
No (n=151)	21.38±12.2	
Additional diseases		
Yes (n=97)	24.2±13.11	0.031*
No (n=77)	20.1±10.85	
MetS		
Yes (n=151)	23.1±12.5	0.043*
No (n=23)	17.6±9.05	

ASRS/T: Adult Attention Deficit Hyperactivity Disorder Self-Report Scale Total score; SD: standard deviation; $\bar{x}$: mean; t: Independent Samples t-test; MetS: Metabolic Syndrome

It was investigated whether the ASRS/T scale scores of T2DM patients varied according to demographic variables. It was demonstrated that those with MetS, concomitant disease, organ involvement, eating disorders, and stress-related eating had statistically higher ASRS/T scores than those without these symptoms.

Table 4. Spearman correlation analysis between ASRS scale scores, metabolic syndrome severity, clinical and biochemical parameters of type 1 and type 2 DM patients

	ASRS/I		ASRS/HI		ASRS/T	
	T1DM	T2DM	T1DM	T2DM	T1DM	T2DM
Age						
r	-0.078	-0.038	-0.069	-0.283	-0.084	-0.120
p	0.636	0.621	0.677	0.016*	0.610	0.115
BMI						
r	-0.066	-0.039	-0.039	0.009	-0.062	0.026
p	0.690	0.614	0.814	0.909	-0.708	0.736
WC						
r	-0.110	-0.059	-0.211	-0.040	-0.173	-0.058
p	0.503	0.440	0.196	0.602	0.291	0.445
HbA1C						
r	0.131	-0.012	0.230	0.075	0.195	0.032
p	0.427	0.874	0.160	0.323	0.233	0.678
Trigliseride						
r	-0.289	0.129	-0.383	0.163	-0.373	0.165
p	0.74	0.091	0.016*	0.032*	0.019*	0.029*
Total cholesterol						
r	-0.166	0.018	-0.372	0.122	-0.286	0.078
p	0.311	0.816	0.020*	0.109	0.077	0.308
HDL						
r	0.157	-0.094	0.061	-0.110	0.133	-0155
p	0.339	0.218	0.714	0.148	0.421	0.130
LDL						
r	-0.101	-0.013	-0.025	0.062	-0.079	0.024
p	0.539	0.863	0.879	0.420	0.633	0.750
AIP						
r	-0.301	0.095	-0.291	0.167	-0.337	0.148
p	0.063	0.212	0.072	0.028*	0.036*	0.051
MetS severity						
r	-0.183	0.271	-0.168	0.306	-0.201	0.311
p	0.265	0.024*	0.307	0.006*	0.221	0.005*

T1DM: Type 1 Diabetes Mellitus, T2DM: Type 2 Diabetes Mellitus, ASRS: Adult Attention Deficit Hyperactivity Disorder Self-Report Scale, ASRS/I: Inattention score, ASRS/HI: Hyperactivity impulsivity score; ASRS/T: Total score, BMI: Body mass index; WC: Waist Circumference HbA1c: Glycosylated haemoglobin; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; AIP: Atherogenic index of Plasma; MetS: Metabolic Syndrome.

Correlation analyses were conducted between ASRS scale scores (attention, hyperactivity, and total scores) and clinical and biochemical parameters such as age, BMI, WC, HBa1c, TGS, Total cholesterol, LDL, PAI, and MetS severity in T1DM and T2DM patients. A moderate negative correlation was detected between ASRS/HI score and TG and total cholesterol (r=-0.383, p=0.016; r=-0.372, p=0.020 respectively), and a moderate negative correlation was detected between ASRS/T score and TG and AIP (r=-0.373, p=0.019; r=-0.337, p=0.036) in T1DM. In T2DM, a moderate negative correlation was detected between age and ASRS/HI (r=-0.283, p=0.016), and a weak positive correlation was detected between ASRS/HI and AIP (r=0.167, p= 0.028). A weak positive correlation was detected between the ASRS/T score and TG in T2DM (r=0.165, p=0.029). In the same table, while no relationship was found between MetS severity and ASRS/D, ASRS/HI, and ASRS/T scores in T1DM, a moderate positive correlation was detected in all ASRS scores in T2DM (r=0.271, p=0.024; r=0.306, p=0.006; r=0.311, p=0.005).

Table 5. Linear regression analysis model for the effect of ASRS-HI and ASRS-total scale score on MetS severity in type 2 DM patients

	B	SE	β	R	p
ASRS-HI	3.32	0.14	0.206	0.206	0.000*
ASRS-T	3.23	0.15	0.211	0.211	0.000*

SE: Standart error, ASRS: Adult Attention Deficit Hyperactivity Disorder Self-Report Scale, ASRS/HI: Hyperactivity impulsivity score; ASRS/T: Total score

In the linear regression analysis model results regarding the effect of ASRS-HI and ASRS-T Scale Score on MetS Severity in T2DM patients, ADHD-HI and T score were statistically effective on the severity of MetS.

Table 6. Comparison of ASRS scores according to DM duration

DM Duration	ASRS/T	ASRS/I	ASRS/HI
1-5 years (n=72)	20.6±12.7	10.5±7.3	10.1±6.6
5-10 years (n=66)	23.9±12.5	12.5±7.3	11.4±6.7
≥10 years (n=75)	25.89±11.5	14.2±6.9	11.6±6.1
p	0.035	0.007*	0.345

*Bonferroni posthoc difference: 1-5 years and ≥10 years (p=0.005); P<0.016 is significant. ASRS: Adult DM: Diabetes Mellitus, Attention Deficit Hyperactivity Disorder Self-Report Scale, ASRS/I: Inattention score, ASRS/HI: Hyperactivity impulsivity score; ASRS/T: Total score

The ASRS/HI score of 213 patients did not vary according to the duration of diabetes, but as the duration of diabetes increased, the ASRS/T and ASRS/I scores gradually increased. ASRS/T score did not show a statistical difference, but there was a statistically significant difference in ASRI/I score in patients with DM for 1-5 years and over ten years (p=0.008).

DISCUSSION

DM is a chronic metabolic disease that negatively impacts carbohydrate, protein, and fat metabolism and might follow a severe course. With its rapidly increasing global prevalence, it has become one of the primary public health issues. Hence, it is imperative to emphasize the need for early detection and intervention in managing this disease while acknowledging the societal obligation to enhance the general knowledge of associated consequences. Recent research has indicated a notable association between ADHD and endocrine and metabolic disorders. Among these disorders, DM has emerged as the most often reported condition in adults with ADHD. In a comprehensive cohort research, it was observed that the prevalence of T2DM was 70% higher among those diagnosed with ADHD than those who did not have ADHD.[26] ADHD has been associated with many adverse health outcomes, including reduced physical activity, binge eating, increased body weight, and insulin resistance. These factors may potentially contribute to the development of MetS and T2DM in affected individuals.

The objective of this study is to explore the frequency of ADHD in type 1 and 2 diabetic patients. Additionally, the study aims to investigate the potential association between ADHD and MetS, AIP, and other lipid parameters. Our research indicated that 10.7% of diabetic patients presented with ADHD symptoms.

In our study, a difference was detected between the T1DM and T2DM groups regarding the ADHD symptoms. It was found that ADHD symptoms were significantly higher in patients with T1DM compared to patients with T2DM. However, the higher ASRS scores in T1DM compared to T2DM might be attributed to different mechanisms. For instance, fluctuations in blood sugar, especially hypoglycemia, can adversely affect brain functions, including attention, concentration, and memory. Chronic hyperglycemia, on the other hand, may damage neuronal functions, intensifying the severity of ADHD symptoms. DM management is more difficult in younger individuals, which might trigger ADHD symptoms and signs.

In a recent study predominantly composed of patients with T2DM, the prevalence of ADHD was found to be 2.4%.[27] In another study, 7.2% of patients with T2DM were diagnosed with ADHD based on the ASRS. In our research, ADHD prevalence in T2DM was found to be 9.8%. In a large meta-analysis, ADHD prevalence in children and adolescents with T1DM was found to be 5.3%.[28] In another study comprising adults with T1DM, ADHD prevalence was 9.5%.[29] In our study, similar to the latter research, adults with T1DM were included, and the ADHD prevalence was a surprisingly elevated 15.4%. Different outcomes in such studies might be possible among different countries, ethnicities, or socioeconomic groups. As can be understood from the tables in our research, all ASRS scale scores were higher in T1DM compared to T2DM, and the likelihood of ADHD diagnosis was also higher in T1DM. In addition, another finding from our study is that the ADHD manifestations in T2DM are mostly inattentive; hyperactivity and impulsivity are more common in T1DM. Due to ADHD presenting differently in young and middle-aged individuals, the lower average age of patients with T1DM compared to those with T2DM in our study might have contributed to the different clinical presentations observed in the two diabetic groups. AIP levels and other metabolic laboratory parameters were lower in T1DM. The younger average age in this group, and consequently the reduced likelihood of accompanying disease that could pose an additional cardiovascular risk, might explain this result. Age, TG, AIP, LDL, Uric Acid, and MetS severity were higher in T2DM, and as MetS severity, PAI, and TGS levels increased, ASRS/HI and total scores also increased. In patients with T2DM, just as with ADHD, there are problems with night eating habits, sleep disturbances, emotional stress, and appetite control. It has been reported that individuals with ADHD have cardiovascular risk twice as high as those without ADHD,[30] just like in DM.[31]

In T2DM, due to higher levels of TG and lower levels of HDL, the AIP level was found to be higher than in T1DM. Additionally, the AIP levels in both groups were found to be above the normal range. In the T2DM group, ASRS-HI and T scores also exhibited a significant effect on the severity of MetS. The increase in TG levels, a primary component of lipotoxicity, which acts as a significant systemic inflammatory stimulator, might cross the blood-brain barrier, potentially causing cerebrovascular inflammation. The positive correlation between ASRS scores and TG and AIP levels in T2DM might be attributable to cerebrovascular inflammation intensifying the ADHD symptoms. The absence of this positive correlation between AIP and ADHD scores in the T1DM group might be due to TG levels being relatively closer to the fact that this positive correlation was not observed in the T1DM group and may be attributed to TG levels being at a normal level.

The prevalence of MetS in the adult population is between 20-25%, whereas it is around 80% in patients with T2DM.[32,33] It was found to be 86.8% in the T2DM group, consistent with these studies in our study. Traditionally, patients with T1DM are believed to have lower BMI and, consequently, a lower risk of MetS.

However, in recent years, the profile of patients with T1DM has been changing rapidly because of increased sedentary lifestyles and intake of energy-dense foods. In a prospective study conducted in patients with T1DM, the prevalence of MetS was 12%.[34] In our study, the prevalence of MetS in the T1DM group was 10.3%. However, in patients with T2DM who have an additional disease, diabetic-related organ involvement, and MetS, the ASRS/T score was significantly higher than those without. Thus, increased oxidative stress and inflammation-induced neuronal degeneration, leading to neurotransmitter metabolism disruptions, may contribute to the development of ADHD, particularly in the presence of genetic factors. In our study, it was also found that as the duration of diabetes increased, the ASRS-Total and Inattention scores increased. This difference was most evident in groups between 1-5 years and above 10 years. There was no relationship between ASRS-HI score and the duration of DM.

This study has some limitations. Firstly, one of these limitations is using self-report scales in our research. Secondly, the cross-sectional nature of our research does not provide sufficient answers regarding causality. However, even if the results do not establish causality, they indicate a strong relationship between DM and ADHD symptoms. However, patients with major psychiatric illnesses and those using psychotropic medications were excluded; the absence of a psychiatric examination can be considered one of the limitations of this study. Although diabetes is inherently a comorbid disease, the exclusion of patients with major comorbidities represents both a strength and a limitation of our study. Despite the limitations, this study also has notable strengths. The enrollment of both type 1 and type 2 diabetic patients, considering BMI, lipid profiles, and the presence and severity of MetS, constitutes the strengths of this study. Additionally, our study results have the potential to contribute to increased self-awareness regarding ADHD symptoms in the diabetic population.

In patients with T1DM, managing glycemic control and adjusting insulin doses by monitoring blood sugar levels may become much more challenging due to ADHD symptoms such as inattention, impulsivity, impairments in planning, and time management skills. Investigating the presence of neuropsychiatric and neurodevelopmental disorders like ADHD provides many benefits in the management. In order to ensure patients' quality of life and metabolic control and even to prevent acute and chronic complications of diabetes, recognizing and treating ADHD symptoms in addition to diabetes management should be considered a medical necessity.

CONCLUSION

The coexistence of DM and ADHD should be recognized as a high-risk population requiring a comprehensive multidisciplinary approach. In addition to the diabetes and ADHD specialists, this team should include a dietitian, social worker, and psychologist. In clinical practice, this holistic approach potentially reduces the risks of acute and chronic complications, including cardiovascular risk, through the enhanced management of DM. The relationship between ADHD, DM, and MetS is an essential issue that deserves further investigation. Therefore, to manage all these diseases, there is a need for more comprehensive and long-term follow-up studies that will guide clinical practices in these fields.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study protocol was approved by the Erzurum Training and Research Hospital Ethics Committee (Date: 14.06.2023, Decision No: 02/16).

Informed Consent

All participants provided written and verbal informed consent.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper and that they have approved the final version.

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